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EXAMINER	
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ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/691,928	GOLDSTEIN ET AL.	
	Examiner	Art Unit	
	Nathan W. Schlientz	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :2/27/04, 7/26/04, 5/21/07, and 7/23/07.

DETAILED ACTION

Status of Claims

Claims 1-17 are pending and are examined herein on the merits for patentability. No claim is allowed at this time.

Withdrawn Rejections

1. The rejection of Claim 1 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for introducing new matter (i.e. recitation of "low-medium potency steroidal inflammatory") is hereby withdrawn by the examiner in light of the instant specification disclosing prednicarbate, desonide, triamcinolone actinide, hydrocortisone butyrate, hydrocortisone probutate, fluocinolone acetonide, and hydrocortisone valerate, which have low-medium potencies depending on the carrier formulation (i.e. ointment, gel, lotion, or cream). The potency of the aforementioned steroidal inflammatory compounds is an inherent property of the compositions and thus Applicant's were in possession of low-medium potency steroids at the time of filing the instant application.

2. The rejection of Claim 1 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for introducing new matter (i.e. "higher potency than 1 wt% hydrocortisone") is hereby withdrawn by the examiner in light of Applicant's argument that a person of ordinary skill in the art would recognize which steroids would have a potency of higher than 1 wt% hydrocortisone.

3. The rejection of Claims 1-17 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention (i.e. recitation of "low-medium potency steroidal inflammatory") is hereby withdrawn by the examiner in light of Applicant's argument that low-medium potency steroids are readily known in the art and recognized by a person of ordinary skill in the art.

4. The rejection of Claims 1-3, 7-10 and 13-17 under 35 U.S.C. 102(e) as being anticipated by US Patent Application Publication 2003/0232086 (McCadden) is hereby withdrawn by the examiner in light the Declaration under 37 C.F.R. § 1.131, filed 14 March 2007.

5. The rejection of Claims 1-3, 7-10, 13 and 17 under 35 U.S.C. 102(b) as being anticipated by US Patent 5,219,877 (Shah et al.) is hereby withdrawn by the examiner in light of Applicant's argument, page 5, lines 14-15, that Shah et al. disclose the potency of the hydrocortisone-17-valerate to be "mid-potency", wherein the instant claims are drawn to low to low-medium potency steroids.

6. The rejection of Claims 1-3, 7-13 and 17 under 35 U.S.C. 102(b) as being anticipated by US Patent 6,075,056 (Quigley et al.) is hereby withdrawn by the examiner

7. The rejection of Claims 4-6, 11 and 12 under 35 U.S.C. 103(a) as being unpatentable over McCadden is hereby withdrawn by the examiner in light of the aforementioned Declaration under 37 C.F.R. § 1.131.

8. The rejection of Claims 4-6 under 35 U.S.C. 103(a) as being unpatentable over Shah et al. is hereby withdrawn by the examiner in light of Applicant's aforementioned argument that Shah et al. disclose the potency of the hydrocortisone-17-valerate to be "mid-potency", wherein the instant claims are drawn to low to low-medium potency steroids.

9. The rejection of Claims 11 and 12 under 35 U.S.C. 103(a) as being unpatentable over Shah et al. in view of Quigley et al. is hereby withdrawn by the examiner in light of Applicant's aforementioned argument that Shah et al. disclose the potency of the hydrocortisone-17-valerate to be "mid-potency", wherein the instant claims are drawn to low to low-medium potency steroids.

10. The rejection of Claims 14-16 under 35 U.S.C. 103(a) as being unpatentable over Shah et al. in view of US Patent 5,686,089 (Mitra et al.) is hereby withdrawn by the examiner in light of Applicant's aforementioned argument that Shah et al. disclose the potency of the hydrocortisone-17-valerate to be "mid-potency", wherein the instant claims are drawn to low to low-medium potency steroids.

11. The rejection of Claims 14-16 under 35 U.S.C. 103(a) as being unpatentable over Shah et al. in view of US Patent 6,444,647 (Robinson et al.) is hereby withdrawn by the examiner in light of Applicant's aforementioned argument that Shah et al. disclose the potency of the hydrocortisone-17-valerate to be "mid-potency", wherein the instant claims are drawn to low to low-medium potency steroids.

Claim Objections

1. Claim 5 is objected to because of the following informalities: the first line states "5.0% wt %". The examiner believes Applicant intended to state "5.0 wt%". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, Claim 3 recites the limitation "wherein R_1, R_2, R_3, and R_4 groups are ..." in the first and second line of the claim. There is insufficient antecedent basis for this limitation in the claim. Claim 3 is dependent from claim 1, which does not provide a structure with R groups. It is believed by the examiner that claim 3 is intended to be dependent from claim 2, as opposed to claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1 and 8-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Quigley et al.

Quigley et al. disclose a lotion having the following composition: water, the solvent propylene glycol, the humectant glycerin, the emulsifier glyceryl monostrearate, the preservatives benzyl alcohol and sodium benzoate, the base triethanolamine, a steroid from about 0.01 to 0.1 wt.%, preferably betamethasone dipropionate (betamethasone dipropionate lotion is a class 5 lower-mid strength potency steroid at 0.02 wt.%, see column 5, line 31), and the antifungal butenafine HCl (column 11, lines 3-23; Table G). Quigley et al. also discloses the anti-fungal compounds include terbinafine and naftifine (column 4, lines 4-51). Quigley et al. further disclose that steroids that penetrate the skin cause undesirable side effects (column 1, lines 28-29), and penetration of the epidermis with the test formulations proved to be significantly lower than that shown for Lotrisone formulation (column 18, lines 38-42). Therefore, Quigley et al. disclose a lotion composition comprising all the limitations of the instant claims and discloses the desire to minimize penetration of the steroid through the epidermis in an attempt to avoid undesirable side effects. Although the composition listed in Table G of Quigley et al. discloses butenafine as the preferred anti-fungal, the disclosure recites three anti-fungals of particular interest: terbinafine, naftifine and butenafine. Therefore, one of ordinary skill in the art would immediately envisage a composition comprising all the ingredients listed in Table G, except substituting terbinafine or naftifine for butenafine.

2. Claims 1-3, 8-13 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 1 159 956 A2 (hereinafter Burnett et al.).

Burnett et al. disclose compositions comprising an anti-fungal (i.e. ketoconazole), a steroidal anti-inflammatory (i.e. desonide), a solvent/penetration enhancer (i.e. propylene glycol), a humectant (i.e. glycerin and/or sorbitol), an emollient (stearyl alcohol or cetyl alcohol), dibasic sodium phosphate, PPG-15 stearyl ether, and benzoic acid (abstract; paragraphs [0002], [0008], [0009], [0012]-[0019]; and Tables 1-4). Burnett et al. further disclose that topical compositions known in the prior art comprise an anti-fungal and steroid have a pH of between 2.5 and 6 (paragraph [0006]). Burnett et al. further disclose treating *Trichophyton rubrum* (i.e. tinea corporis, tinea cruris and tinea pedis) with the compositions of their invention (paragraph [0032]).

It is noted that Burnett et al. disclose the required penetration enhancer/solvent selected from the group consisting of alcohol, propylene glycol, or a combination thereof (paragraph [0012]), wherein the instant invention requires the composition does not cause the steroids to penetrate the skin and cause undesirable side effects (instant claim 1). However, propylene glycol is a solvent listed in the instant claim 12. Also, Burnett et al. disclose that the compositions of their invention demonstrate targeted delivery of desonide to the skin (cutaneous compartments) with greater amounts of the medicaments in the intended sites of the epidermis and dermis (paragraph [0036]). Burnett et al. state that the compositions demonstrated positively less permeation through the skin into the receptor that could clinically translate into lower systemic toxicity (paragraph [0037]). Therefore, even though Burnett et al. refer to the solvent

propylene glycol (same as instantly claimed) as a penetration enhancer/solvent, they clarify the desire to prevent permeation of the medicament through the skin and into the receptor, resulting in diminished side effects. Thus, the compositions of Burnett et al. are disclosed not to penetrate through the skin and into the receptor.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1,148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 2-3, 7 and 14-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Quigley et al. as evidenced by the instant specification.

Applicant claims:

Applicant claims a topical antifungal composition comprising an anti-fungal, a low to low-medium potency non-halogenated steroidal anti-inflammatory (listed in claim 7),

and a carrier that does not afford penetration of the steroid through the skin causing undesirable side effects. Applicant further claims a method of treating a fungal disease (listed in claim 16) comprising administering the aforementioned composition with a thin application of the composition two times per day to the affected areas, wherein the patient may comprise a child of under 10 years old (claim 15).

Determination of the scope and content of the prior art

(MPEP 2141.01)

Quigley et al. teach a lotion composition comprising an anti-fungal, a low-mid strength steroidal anti-inflammatory (0.01 to 0.1 wt.% betamethasone dipropionate lotion), and excipients that don't afford steroidal penetration of the epidermis, as discussed above. Quigley et al. also teach a cream formulation comprising the same excipients as listed in the aforementioned lotion, wherein the steroid is preferably from 0.01 to 0.1 wt.%, and is preferably betamethasone dipropionate (column 7, line 38 through column 8, line 28; Table A).

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

Quigley et al. do not explicitly teach a composition comprising a low to low-medium potency steroidal anti-inflammatory having a structure shown in instant claim 2, nor those selected from the group listed in claim 7. However, Quigley et al. teach desonide cream 0.05% as a suitable steroid anti-inflammatory for use in the present invention (column 5, line 45; and column 8, lines 23-24). Desonide is a species within

the generic structure of steroid anti-inflammatory compounds shown in instant claim 2 (instant claims 2-5).

Also, Quigley et al. do not explicitly teach applying the composition two times per day to the affected area. However, Quigley et al. teach that routine experimentation by one of ordinary skill in the art would be able to determine the effective amount of application of the topical composition (column 7, lines 11-24).

Furthermore, Quigley et al. do not teach applying the composition to a child of under 10 years old. However, Quigley et al. teach desonide cream 0.05% as a suitable steroidal anti-inflammatory and the instant specification teaches that desonide is a class 6 non-fluorinated topical corticosteroid which has been available for more than two decades and clinical trials have shown that desonide is effective and safe for treating children having dermatosis or other skin diseases.

Finding of *prima facie* obviousness

Rational and Motivation (MPEP 2142-43)

Therefore, it would have been *prima facie* obvious for one skilled in the art at the time of the invention to use desonide cream 0.05% in the cream formulation taught by Quigley et al. because Quigley et al. teach that desonide cream 0.05% is a suitable steroidal anti-inflammatory for use in combination with an antifungal. One of ordinary skill in the art would have been motivated to use desonide cream 0.05% in the cream formulation of Quigley et al. because desonide is a class 6 non-fluorinated topical corticosteroid which has been available for more than two decades and clinical trials have shown that desonide is effective and safe for treating children having dermatosis

or other skin diseases, as evidenced by the instant applications specification. Also, it would have been routine experimentation for a person of ordinary skill in the art to determine the number of applications of the cream formulation of Quigley et al. in order to achieve desired results in treating fungal diseases.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

2. Claims 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Burnett et al. in view of U.S. Patent No. 5,219,877 (hereinafter Shah et al.).

Applicant claims:

Applicant claims a topical antifungal composition comprising 0.1 to 5.0 wt.% clotrimazole, 0.01 to 5.0 wt.% desonide, and a carrier that does not afford penetration of the steroid through the skin causing undesirable side effects.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Burnett et al. teach compositions comprising preferably about 0.05 wt.% desonide ([paragraph [0019]) and preferably about 2 wt.% of an imidazole anti-fungal agent (paragraphs [0014] and [0019]), wherein the composition does not permeate through the skin, as discussed above.

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

Burnett et al. do not teach the anti-fungal agent to comprise clotrimazole. However, Shah et al. teach formulations suitable for treatment of tinea capitis, tinea corporis, tinea cruris, and tinea pedis comprising 0.2 to 2.0% w/v of an imidazole anti-fungal agents, such as clotrimazole, and further comprising an anti-inflammatory steroid including desonide (column 1, lines 6-14; and column 3, lines 43-65). Shah et al. further teach that commercially marketed 1 wt.% clotrimazole exhibits very low permeation rates through skin, and cannot be effectively used for treatment of deep skin fungal infections (column 6, lines 3-34). Thus, the commercially marketed clotrimazole does not permeate through the skin.

Finding of *prima facie* obviousness

Rational and Motivation (MPEP 2142-43)

Therefore, it would have been *prima facie* obvious for one skilled in the art at the time of the invention to use clotrimazole as the imidazole anti-fungal agent in the compositions of Burnett et al. because Shah et al. teach clotrimazole as a suitable imidazole anti-fungal for treating tinea capitis, tinea corporis, tinea cruris, and tinea pedis. One would have been motivated to use clotrimazole as the anti-fungal agent because Burnett et al. teaches the desire to reduce the amount of skin permeation in order to reduce side effects, and Shah et al. teach that commercially marketed 1 wt.% clotrimazole does not permeate through the skin.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

1. Applicant's Remarks filed 14 March 2007 and 21 May 2007 have been considered but are moot in view of the new grounds of rejection.

2. Applicant's Remarks filed 30 July 2007 have been fully considered, but are not found to be persuasive.

Applicant's argue on page 6 of the aforementioned Remarks filed 30 July 2007 that Burnett et al. describe formulations which require the use of a penetration enhancer, wherein the instant specification and instant claim 1 teaches away from a formulation where the anti-inflammatory penetrates into the dermis. However, the examiner fully considered the disclosure of the instant specification and concluded that the statement "Steroids can penetrate the skin and cause undesirable side effects, including..." does not teach away from the disclosure of Burnett et al. Burnett et al. also disclose the desire to prevent permeation through the skin in an attempt to prevent side effects by lowering systemic drug toxicity (paragraphs [0036] and [0037]).

Furthermore, the instant specification doesn't disclose that penetration into the dermis is the cause of the side effects, but merely that steroids can penetrate the skin

and cause side effects. Burnett et al. also teach that steroid penetration of the skin can cause side effects and their compositions reduce the amount of penetration and permeation through the skin into the receptor, thus reducing the systemic toxicity. Therefore, to the extent the instant specification discloses the desire to prevent penetration of steroids through the skin, Burnett et al. also discloses the same desire and compositions for achieving reduced systemic toxicity.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan W. Schlientz whose telephone number is 571-272-9924. The examiner can normally be reached on 8:30 AM to 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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